

REMARKS/ARGUMENTS

Claims 1-3, 5-6, 8, 10-23, 25-27, 31-33, 46, 50, 53, and 60-62 are pending in this application. Claims 4, 7, 9, 24, 28-30, 34-45, 47-49, 51-52, and 54-59 are canceled without prejudice. New claims 60-62 are added.

I. Status of the claims

Claims 1, 2, 5, 10, 13, 20-23, 26, and 46 are amended, and new claims 60-62 are added to recite "lipid binding protein-7" or "lbp-7." The claims are also amended to recite the nucleic acid that encodes the lbp-7 polypeptide, "T22G5.2." Support for these amendments is found throughout the specification, for example, at Tables 3, 6, and 8 and original claim 1. Claims 1 and 21 are amended to recite specific stringent hybridization conditions. Support for these amendments is found throughout the specification, for example, at page 28, lines 18-20. Claims 1 and 21 are also amended to recite hybridization to the complement of the T22G5.2 nucleic acid. Support for these amendments is found throughout the specification, for example, at page 18, lines 24-27 and page 24, lines 25-27. Claims 1, 21, 46, and new claim 60 now recite comparison of the effect of a compound to a control. Support for these amendments is found throughout the specification, for example, at page 21, lines 15-23. Claims 3, 13, 23, and new claim 61 are amended to recite that the lbp-7 protein binds fatty acids. Support for these amendments is found throughout the specification, for example, at Tables 3, 6, and 8. Claims 5, 25, and new claim 62 recite the transcriptional phenotype of Group 2 genes identified in this application, *i.e.*, "transcription of the nucleic acid is increased when daf-16 activity is inhibited and is decreased when daf-2 activity is inhibited." Support for these amendments is found throughout the specification, for example, at page 69, lines 1-4. In addition, T22G5.2 is identified as a class 2 gene in table 6. Claims 27 is amended to include RNAi molecules. Support for these amendments is found throughout the specification, for example, at page 53, line 30 through page 54, line 1. These amendments add no new matter.

New claim 60 recites the method steps of claim 1, but identifies the lbp-7 polypeptide by % identity to a reference sequence. New claim 61 recites the method steps of

claim 21, but identifies the lbp-7 polypeptide by % identity to a reference sequence. Support for these amendments is found throughout the specification, for example, at original claims 1 and 21, and at page 22, lines 21-30. New claim 62 recites the method steps of claim 46, but identifies the lbp-7 polypeptide as encoded by a nucleic acid that hybridizes to a reference sequence. Support for this amendment is found throughout the specification, for example, at original claim 46, and at page 18, lines 24-27; page 24, lines 25-27; page 28, lines 18-20. These amendments add no new matter.

II. Objections to the specification

According to the Office Action, Tables 2-8 do not have a clear title or description. In order to expedite prosecution, the specification is amended at page 12 to describe the tables. Support for this amendments is found, *e.g.*, in Tables 2-8.

III. Objections to the claims

Claims 1-33, 46, and 50-53 are objected because they allegedly contain non-elected subject matter. The claims are now amended to recite T22G5.2 or an lbp-7 protein encoded by the T22G5.2 sequence. In view of these amendments, withdrawal of the claim objections is respectfully requested.

IV. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1-33, 46, and 50-53 are rejected because the specification allegedly fails to convey to those of skill that the inventors had possession of the invention as of the filing date. The Office Action alleges that the claimed genus of polypeptides is large and encompasses polypeptides that potentially do not share the same function as the encoded lbp-7 protein. The Office Action also alleges that the specification does not describe all the polypeptides encoded by nucleic acids that hybridizes to the T22G5.2 nucleic acid sequence.

To the extent the rejection applies to the amended claims, Applicants respectfully traverse. As currently applied, the specification does comply with U.S. patent law for description of an amino acid sequence. The Federal Circuit Court of Appeals has addressed the

level of description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. See, *e.g.*, *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). As alluded to by the Examiner, an applicant may show that an invention is complete by

. . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

First, the specification as filed does disclose functional characteristics of the encoded lbp-7 protein. The function of the protein is disclosed in Tables 3, 6, and 8, which describe the lbp-7 protein as a fatty acid binding protein. Moreover, expression of the T22G5.2 nucleic acid that encodes the lbp-7 protein is regulated in an age dependent manner. The T22G5.2 nucleic acid was identified as a member of the Group 2 genes, *i.e.*, nucleic acids whose transcription is decreased in *daf-2* minus genetic background, but is increased in a *daf-2*, *daf-16* double mutant. These functions are required in the lbp-7 proteins recited in amended claims 3, 5, 22, 23, 61, and 62.

The Office Action also alleges that the number of sequences encompassed by claims that recite hybridization language is large and potentially may encode polypeptides with a function that differs from that of the lbp-7 polypeptide. Applicants respectfully traverse. The claims recite specific stringent hybridization conditions, in specific buffers, performed at specific temperatures. These stringent conditions limit the number of sequences that can hybridize to the full length of the recited T22G5.2 nucleic acid. In addition, as functional requirements for the lbp-7 proteins are now recited in the claims, at a minimum, claims 3, 5, 22, 23, 61, and 62, are not subject to this rejection.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." See, *e.g.*, 66 Fed. Reg. 1099, 1106 (2001). In *Falkner v. Inglis*, the

Federal Circuit ruled that, for claims to nucleic acid sequences, and by analogy to amino acid sequences, absence of examples does not render written description inadequate and that actual reduction to practice is not required. *See, e.g., Falkner v. Inglis*, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006).

The Examiner appears to be concerned about the amount of structural information provided for the recited nucleic acid and amino acid sequences. In response, Applicants assert that disclosure of every single gene or amino acid sequence is simply not required to meet the written description requirement. Other distinguishing characteristics can be used to describe a nucleic acid or amino acid sequence. "As explained by the Federal Circuit, '(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.'" MPEP 2163.II.A.3(a), *citing Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006).

The T22G5.2 nucleic acid and the encoded lbp-7 polypeptide are from the organism *C. elegans*. The *C. elegans* genome was sequenced and published in 1998 and the sequence of the nucleic acids and encoded proteins are found in sequence data bases. *See, e.g.*, GenBank accession number Z81127, which has the sequence of the full T22G5 cosmid and is included herein as Exhibit A. This publicly available source was easily accessible to those of skill, based on information in the specification. Thus, using publicly available sequence information and the specification, those of skill would recognize that the inventors had possession of the invention at the time of filing.

The present application provides the first evidence that the T22G5.2 gene and its encoded lbp-7 protein regulate aging, using, *e.g.*, mRNA expression data and RNAi analysis. The claims are directed to methods of identifying modulators of aging by identifying modulators of the lbp-7 protein activity or expression. As the structures of the T22G5.2 nucleic acid sequence and the lbp-7 amino acid sequence were known at the time of filing, the written description requirement is met.

With regard to claims that recite an lbp-7 polypeptide with a specified percent identity to a reference sequence, *i.e.*, claims 46, 60, 61, and dependent claims, thereof, Applicants assert that these claims comport with the with the Revised Written Description Training Materials, issued March 25, 2008. Applicants respectfully direct the Examiner's attention to claim 1 of Example 11A in the Written Description Training Materials (page 37). Exemplary claim 1 reads "An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2." The training materials note that "There is no functional limitation on the nucleic acids of claim 1 other than that they encode the polypeptide of SEQ ID NO: 2 or any polypeptide having 85% structural identity to SEQ ID NO: 2. The genetic code and its redundancies were known in the art before the application was filed." The Training Materials explain that exemplary claim 1 satisfies the written description requirement, reasoning "The disclosure of SEQ ID NO: 2 combined with the pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. With the aid of a computer, one of skill in the art could have identified all of the nucleic acids that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. Thus, one of ordinary skill in the art would conclude that the applicant was in possession of the claimed genus at the time the application was filed." Based on Example 11A of the revised Written Description Training Materials, Applicants believe that, at a minimum, claims 46, 60, 61, and dependent claims, thereof, satisfy the Written Description Requirement.

With regard to the claims that recite an lbp-7 protein encoded by a nucleic acid that hybridizes under high stringency conditions to the complement of a reference sequence, *i.e.*, claims 1, 21, and 62, Example 6 of the revised Written Description Training Materials discusses claims that recite hybridization conditions. The sample claims provided in that example do not include a claim that recites high stringency hybridization conditions *without* the recitation of function. However, Example 6 (at page 22) does state:

Because hybridization under highly stringent conditions requires a high degree of structural complementarity, nucleic acids that hybridize to the complement of SEQ ID NO:1 must share many nucleic acids in common with SEQ ID NO:1. Thus, the claimed

genus necessarily includes partial structures of SEQ ID NO:1.
The disclosure of SEQ ID NO:1 combined with the knowledge in the art regarding hybridization **would put one in possession of the genus of nucleic acids that would hybridize under stringent conditions** to SEQ ID NO:1. (emphasis added)

Thus, based on this explicit guidance in Example 6 of the training materials, and, by analogy, the guidance provided by Example 11A of the training materials, discussed above, Applicants assert that claims 1, 21, and 62 (and their dependencies) satisfy the written description guidelines.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of written description is respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1-33, 46, and 50-53 are rejected because the specification allegedly fails to enable one of skill to make and/or use the invention. To the extent the rejection is applied to the amended claims, Applicants respectfully traverse the rejection. The Office Action discusses a number of the Wands factors. Applicants address each factor, in turn, below.

A. The nature of the invention

The invention is a method of identifying compounds that modulate aging by identifying compounds that modulate activity of the lbp-1 polypeptide.

B. The breadth of the claims

The Office Action alleges that the breadth of the claims is very broad because of hybridization language, use of the terms homolog or ortholog, and because the functional effect is allegedly not specified. Applicants direct the Examiner's attention to the amended claims, which recite specific hybridization conditions or percent identity to a reference sequence, and no longer recite homolog or ortholog. The claims also recite that, in order to identify a compound that modulates aging, the effect of the compound must be different than a control sample. The breadth of the amended claims meets the enablement requirement.

C. The teaching of the specification

According to the Office Action, the specification fails to explain how to identify a compound that can modulate aging simply by contacting it with the lbp-7 polypeptide and fails to indicate what type of functional effect is determined that indicates a compound modulates aging. Office Action at page 6. Applicants respectfully disagree.

The Office Action alleges that the role in aging played by the lbp-7 protein and its encoding nucleic acid is not explained by the specification. This allegation is incorrect. The specification does provide evidence of a role in aging for the lbp-7 protein and its encoding nucleic acid and provides a method to identify compounds that modulate the lbp-7 role in aging.

As the Office Action indicates, T22G5.2, the nucleic acid that encodes the lbp-7 polypeptide is differentially regulated in daf2 or daf16 genetic backgrounds. This data is shown in Table 6, which classifies T22G5.2 as a Class 2 gene. Tables 3 and 8 provide data that demonstrates the role in aging played by the T22G5.2 nucleic acid and its encoded protein, *i.e.*, the lbp-7 polypeptide. Table 8(h) shows the results of lifespan analysis in *C. elegans* that express an RNAi molecule is specific for T22G5.2, preventing its stable expression and expression of the encoded lbp-7 protein. Decreased stability of T22G5.2 mRNA and thus, inhibition of the encoded lbp-7 polypeptide expression and activity, led to an increase in lifespan in certain genetic backgrounds, as compared to a vector control. Moreover, the T22G5.2-specific RNAi molecule is a compound that modulates aging by modulating the activity or expression of the encoded lbp-7 protein. Thus, the specification provides both instruction to identify and an example of a compound that modulates aging, using the method steps that are recited in the claims. As RNAi negatively regulates its target, it follows that inhibition of the activity of the lbp-7 polypeptide will similarly modulate aging. Thus, those of skill recognize that identification of compounds that modulate lbp-7 activity, *i.e.*, by contacting a test compound with the lbp-7 protein, will allow identification of compounds that modulate aging.

D. The state of the art and level of unpredictability in the art

According to the Office Action, the specification fails to explain how to identify a compound that can modulate aging simply by contacting it with the lbp-7 polypeptide. The Office Action also alleges that the specification fails to teach mammalian homologues or orthologs. Office Action at pages 6-7. Applicants respectfully disagree. In order to expedite prosecution, language related to mammalian homologues or orthologs has been deleted from the claims.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

VI. Rejections under 35 U.S.C. §112, second paragraph

Claims 7, 11, 21-33, 51 and 52 are rejected as allegedly indefinite. To the extent the rejections apply to the amended claims, Applicants respectfully traverse the rejection.

Claim 7 is amended for recitation of "enzymatic activity." in order to expedite prosecution, claim 7 is now amended.

Claim 11 is rejected for use of the word "derived." In order to expedite prosecution, claim 7 is amended to delete the word "derived."

Claim 21 and dependent claims 22-33 are rejected for reciting "contacting a host or host cell expressing the protein and evaluating an age associated parameter" because it is allegedly unclear what is used to contact the host or host cell. In order to expedite prosecution, claim 21 is amended to clarify that the host or host cell is contacted with the compound.

Claims 51 and 52 are rejected for recitation of "the criterion is a preselected value" and "a preselected statistical significance", respectively. In order to expedite prosecution, claims 51 and 52 are canceled.

In view of the above amendments and remarks, withdrawal of the rejections for alleged indefiniteness is respectfully requested.

Appl. No. 10/536,635
Amdt. dated May 9, 2008
Reply to Office Action of January 10, 2008

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.


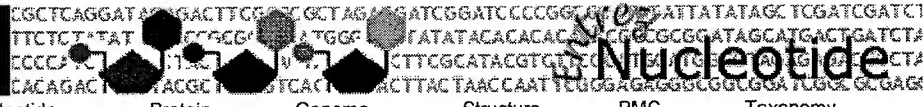
Respectfully submitted,



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BLK:blk
61343450 v1

Exhibit A

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Display 5 ☐ sequence ☐ all but gene, CDS and mRNA

Range: from to ☐ Reverse complemented strand Features:

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 VERSION Z81127.1 GI:1628229
 KEYWORDS HTG.
 SOURCE *Caenorhabditis elegans*
 ORGANISM *Caenorhabditis elegans*
 Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida;
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 REFERENCE 1 (bases 1 to 22254)
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 TITLE Genome sequence of the nematode *C. elegans*: a platform for
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 JOURNAL Science 282 (5396), 2012-2018 (1998)
 PUBMED 9851916
 REMARK Erratum:[Science 1999 Jan 1;283(5398):35]
 REFERENCE 2 (bases 1 to 22254)
 AUTHORS Smye, R.
 TITLE Direct Submission
 JOURNAL Submitted (21-OCT-1996) Nematode Sequencing Project, Sanger
 Institute, Hinxton, Cambridge CB10 1SA, England and Department of
 Genetics, Washington University, St. Louis, MO 63110, USA. E-mail:
 worm@sanger.ac.uk
 COMMENT Coding sequences below are predicted from computer analysis, using
 predictions from Genefinder (P. Green, U. Washington), and other
 available information.
 Current sequence finishing criteria for the *C. elegans* genome
 sequencing consortium are that all bases are either sequenced
 unambiguously on both strands, or on a single strand with both a
 dye primer and dye terminator reaction, from distinct subclones.
 Exceptions are indicated by an explicit note.
 IMPORTANT: This sequence is NOT necessarily the entire insert of
 the specified clone. It may be shorter because we only sequence
 overlapping sections once, or longer because we arrange for a small
 overlap between neighbouring submissions.
 For a graphical representation of this sequence and its analysis
 see:- [http://www.wormbase.org/perl/ace/elegans/seq/sequence?](http://www.wormbase.org/perl/ace/elegans/seq/sequence?name=T22G5;class=Sequence)
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 It may be shorter because we only sequence overlapping sections
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 neighbouring submissions.
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right end of clone T22G5 is at 10221 in sequence Z77652.

The true left end of clone C06B3 is at 22153 in this sequence. The true right end of clone F09F3 is at 2384 in this sequence. The start of this sequence (1..104) overlaps with the end of sequence Z81056.

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